TREATMENT OF PARESIS; ITS LIMITATIONS AND EXPECTATIONS.

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The "*treatment of paresis,*" as a subject for discussion, presents itself, at first sight, as difficult and uninspiring in view of its hopelessness. But I am asked to speak especially of the "*limitations and expectations*" of treatment; this leads the way to a field of inquiry in which lie some of the profoundest problems in medicine. The time now available being brief, I shall speak of our present unsatisfactory means of treatment of a disease as yet regarded as incurable, only to indicate the *limitations* under which we labor.

The diagnosis being made, the prognosis being a fatal ending usually after two to four years in which the manifestations of the disease have been recognized, we are limited to measures for palliating its consequences. The patient needs immediate protection when the onset of the disease is an acute attack of melancholia or mania; when the dementia comes on insidiously, protection is equally important of the personal and business interests both of the patient and his family. Custodial measures become therapeutic together with treatment of general symptoms, when remissions are promoted through improvement in physical health and strength, neurasthenic conditions being especially characteristic of the prodromic and early stages of the disease. The prescribed method always includes "tonics" in all appropriate forms, and a generous diet with interdiction of alcohol. Hydrotherapeutics, now coming into more general use, are often beneficial.

It is aside from all these generally indicated expedients for the management of the cases that the real therapeutic problem arises and baffles our art. The psychiatrist finds himself here in a remarkable position; it is that of being confronted by a well-defined mental disease-form, with concurrent physical signs

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more distinctive than in any other mental disease. These point, by both sensory and motor symptoms, to lesions of the nervous system that show a recognizable underlying disease-process with progressive structural changes producing chiefly extensive degeneration of the nervous system. More than in any other of the true mental diseases, which are such because the mental symptoms essentially constitute the disease-form, have researches in anatomical pathology been possible in the attempts to find an explanation of the mental symptoms. But, for some recent years, little advancement of our knowledge in this direction has been made. Therefore the psychiatrist, who must really do his clinical work from the standpoint of the general physician, has found a barren field of *limitations* for his therapeutic guides when he turns to neurological histology and pathological findings. This is a most significant fact, for, so far as this line of research can go, we are likely to come to the same limits in other forms of mental disease should there ever be discovered concomitant structural changes characteristic of them. The pathological anatomist as our pioneer leads us to this frontier of our realm,—to the Castle Mystery, and lays siege to it; when he fails to carry it by assault, he saps and mines, and employs the strategy of hypothesis, spies of subtle inference and arrows of swift conjecture, often Parthian arrows indeed. Still we wait before the impenetrable wall of our difficulty. It is with us, both in general medicine and psychiatry, much as it was with our fathers when they said the signs of inflammation were heat, redness and swelling. The work of penetration into that which underlies has gone deeper, but our attitude of inquiry remaining precisely the same, we have the superficial replaced by the parenchymatous. We are reaching the limits of knowledge through the study of change in structural form and appearances to the eye; the infinitesimal becomes the insurmountable. We are learning that, inasmuch as psychology and physiology can tell us nothing to explain the normal mechanism of mental activities, we can not expect to see, through the microscope, an explanation of disordered thought and feeling.

It would be a cause of great regret on my part if there should seem to be any disposition, in the hospital work which I represent, to diminish in the least the importance of research in patho-

132.1
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logical anatomy. But there are reasons for seeking an explanation of our clinical problems in the still deeper underlying plane of physiological chemistry. Let me quote from a statement made from this point of view.[1] "That microscopically visible structural changes in any tissue, or in the cells of any tissue, must be preceded by more or less pronounced metabolic changes is surely self-evident. Metabolic changes are chemical changes. Chemical changes are the physical exchanges and transformations that take place in the physical units of matter—the molecules; and the molecules are beyond the ken of the microscopist."

Turning now to aetiology in accordance with the principles of general medicine, we find limitations in the logic of treatment under the leading conceptions of the aetiological factors of paresis which are syphilis and heredity, with alcohol and the stress of modern life contributing. Following the guidance offered by these factors it has been common, outside of the hospitals, when the diagnosis is made and there is a suspicion of syphilis, to treat the cases with mercurials and iodides; in the hospitals this is found to be so futile and even harmful that the practice advocated by many alienists is generally followed in using antisyphilitic treatment only when active syphilis is present. With respect to heredity authorities differ. Our experience at the McLean Hospital agrees with that of many observers in the evidence it gives that paresis is due less to heredity than other forms of insanity. The rôle of heredity, in whatever relation it may bear to insanity in general, is that of inducing a constitutional instability. This neuropathic weakness when transmitted from a syphilitic parentage, or when induced as a sequel to an acquired syphilis, is regarded as having a like influence with stress from excessive mental activity. These predisposing factors working together tend to determine which part of the overworked mechanism is to yield to the active cause of the paretic disease. Alcohol may be a contributing factor also by reducing the normal resistance to morbid influences. In these ways comes the conception of neurasthenic conditions, constitutional or acquired, as having an intimate relation with the onset

[1] Dr. Otto Folin, Chemical Laboratory, McLean Hospital. Notes on relation of pathological chemistry to pathological anatomy.

and course of the disease-process. Hence arise questions of early differential diagnosis between neurasthenia and paresis. Undoubtedly a neurasthenia may be the first to appear, when it is only the effect, and not a part of the cause, of the still unrecognized general paralysis. A history of syphilis always excites suspicion. Out of these aetiological considerations we get, so far, no clearer guides for treatment; antisyphilitic measures, theoretically indicated, fail, and we are left to deal with a general and very empirical conception of neurasthenia.

The history of the course that has been taken by the study of this problem leads to an interesting field. While the *limitations* of our therapeutics continue to be apparent, I can now enter upon the second part of my subject—the *expectations* of treatment. That paresis has its chiefest cause in specific disease is not a conclusion from any discoverable relations between known specific and paretic lesions. The arguments deal with the prevalence in cases of paresis of a history of acquired syphilitic infection, or of its inherited effects. This doctrine is gaining ground, although some authorities demur; it is argued that syphilis not being proven in many cases it should be held not as an essential but only a predisposing cause. Krafft-Ebing's dictum that general paralysis is a product of civilization and syphilization, and Oppenheim's statement that paresis is the outcome of stress and syphilis, give expression to opinions that indicate no more than a sequence of facts, showing the frequency with which specific infection is followed by paresis. As explanatory of a probable real connection in the pathology of these two diseases, it is becoming generally assumed that there is some intervening factor, or condition, that unites them. Oppenheim points to this in making the distinction that people without syphilis, but who are the subjects of mental stress, excitement and excesses, are liable to develop neurasthenia; the syphilitic neurasthenic, however, is liable to dementia paralytica. That there may, or must be, an intermediate element between the two diseases is now either intimated or assumed by most writers, and alike by the advocates of the two leading theories of their pathogenesis relating respectively to the nervous and the vascular systems. We need not dwell upon the arguments for the opposing hypotheses, as to which is first in the disease-process, because they refer alike to

the toxaemias as intervening factors. Though still hypothetical this indicates, at least, the trend of the time in medicine.

We come now to the subject that is of prime importance in our discussion of *expectations* in the treatment of paresis, and of our grounds for them; our problem lies distinctly in the field of general medicine putting the general physician and psychiatrist in precisely the same position toward it. It is not my part here to discuss the pathology of this disease, but it may be permissible to cite briefly some authoritative statements that set forth the aspects of the problem which I wish to consider.

Dr. Mott in the Archives of Neurology for 1899, indicating his reasons for supposing that paresis is a primary degeneration of the neurone with secondary inflammatory changes, says, in other words, that "it is a parenchymatous degeneration due to a loss of durability of the nerve-cell—a premature decay of tissue in which inherited and acquired conditions take part, with the result that progressive death of the latest and most highly developed nervous structures ensues as soon as their initial energy is unable to cope with the antagonistic influences of environment."

Kraepelin,[2] regarding the changes in the nerve parenchyma as the primary alteration, thinks that the microscopic pictures of paretic lesions indicate intoxication. He says that everything points to a grave nutritional disorder, and that the disease is analogous to myxoedema, diabetes, osteomalacia, acromegaly, and the like; he suggests that we have to assume an intervening element between syphilis and paresis, just as we have, for example, a myxoedema develop when the thyroid becomes destroyed by tuberculosis.

Wernicke,[3] regarding a primary destruction, or necrosis, of the nerve tissue, analogous to the degenerative neuritis in the peripheral nervous system, as the primary process, says the paralytic aetiology resembles most the action of poisons. But in general paralysis we must assume that the poison is constantly being produced in the body, as the progressive fatal characteristics can not be otherwise explained. This poison must be metasyphilitic, yet we must assume a bacterial action as the basis

[2] Psychiatrie, 6th ed. Leipzig, 1899.

[3] Grundriss der Psychiatrie, 1900, Leipzig.

of the peculiar condition. The purport of this is that, as in other progressive remitting diseases, the acute and quiescent phases of paresis represent, respectively, the resistive reaction of the body to some toxin, and remissions of its activity indicating cessation of the toxaemia. The views of authorities generally harmonize with the conception of intervening factors. These may, of course, have their place outside of, as well as in, the nervous system itself, and elsewhere in the body. Although such representative opinions do not yet furnish us with guides to treatment, as they hardly take us beyond the stage of hypothesis, yet, nevertheless, they point to a toxaemic origin in the pathogenesis. Thus we as psychiatrists find ourselves engaged in the general movement of the time; and sharing in the great advancement in general medicine we are encouraged in our expectations of things hoped for, in our special field of mental medicine.

On the common ground of general medicine, it is of interest to refer to a statement, made from this point of view by Sir Dyce Duckworth, of the principles upon which our new position is based. In an address, in November, 1900, to the British Medico-Psychological Association on "Mental Disorders Dependent on Toxaemia" he expressed the generally accepted opinions. He said that toxaemic states have been long recognized as clinical features of disease, and the sources of them are as varied as are the separate toxic elements which induce them. Progress in physiological chemistry and bacteriology has now furnished us with the means to explain these conditions. Referring to the action of auto-intoxications in disturbing the harmony of intimate brain-cell metabolism, he noted the deliria of many febrile conditions as examples of distinct toxic infections. After mentioning myxoedema as leading, in like manner, to mental disorders resulting from altered metabolism due to deficient thyroidal influence, it is stated that general paralysis is now regarded as coming into the category of auto-intoxications. His suggestion as to the course of the pathogenesis is one of the interesting variations of the hypothesis. Syphilis although the common antecedent of paresis does not, however, provide the toxin, and we must therefore view its part in the aetiology as leading to progressive degenerative nervous changes, which in turn so modify the inti-

mate metabolism of the tissues as to set free toxic elements. As the various toxic agents which gain admission to the circulation manifest elective affinities for particular systems of neurons, hence the varied results of perverted nutrition and metabolism with the production of new toxins. While these fields of study are yet much unexplored, there are many investigators in them, and here and there knowledge is gained that guides to treatment.

We have now come in this discussion, nearly to its ending, yet upon the grounds so far considered we find ourselves still in the region of hypotheses with waiting expectations of new light upon the treatment of paresis, but with reasonable faith in their final realization. To this practical end, indeed, we may be nearer than has yet been supposed. A new phase of the problem has been presented in contributions by Dr. Bruce, and Dr. Ford Robertson at a meeting, last June, of the Medico-Chirurgical Society of Edinburgh. Dr. Bruce, in his observations of paresis for a number of years noted the common occurrence of gastric and intestinal disorders, with exacerbations accompanied by rise of temperature and hyperleucocytosis. He suspected a toxaemia due to intestinal bacteria. Obtaining blood-serum by wet cupping for lumbago from a paretic patient having a well-marked remission in the second stage, he treated two earlier progressing cases with subcutaneous injections daily for three weeks. The result was complete remissions in both cases then of two years duration. Further experiments are in progress, to procure blood-serum from a horse immunized to bacillus coli. Dr. Bruce believes that small subcutaneous injections of such serum, for three weeks or a month may produce artificial remissions of this disease. His conclusions are:

1. General paralysis is a disease directly due to poisoning by the toxins of bacteria whose point of attack is through the gastric and intestinal mucous membrane.

2. The poisoning is probably a mixed poisoning, but the bacillus coli is apparently one of the noxious organisms.

3. The result of treatment with serum, taken from a case of general paralysis in a condition of remission and injected subcutaneously into an early progressive case, points strongly to the fact that some form of serum treatment is the proper treatment for this as yet incurable disease.

Dr. Robertson, in his observations upon this subject, referring to Dr. Bruce's cases, takes the position, contrary to the opinions already cited, as to pathogenesis, that the theory of the existence of chronic toxaemia is virtually a farther elaboration of the view that the cerebral vascular lesions constitute the first anatomical alteration in general paralysis. He cites authorities defending this view and reaches the following conclusions:

General paralysis is dependent upon the occurrence of chronic toxaemia of gastro-intestinal origin; the toxins are mainly bacterial and are formed in consequence of a partial breakdown of those forces by which the harmful development of the microorganisms that constitute the ordinary flora of the alimentary tract is normally prevented; the toxins are absorbed and tend specially to produce proliferative and degenerative changes in the vessels of the central nervous system, and these vascular changes tend to set in earliest in those parts of the brain that are relatively best supplied with blood, because their walls are brought in contact with the largest quantities of toxins. The part played by syphilis in the pathogenesis of general paralysis and tabes dorsalis is essentially that of altering the natural immunity; and the treatment should be directed primarily to the correction of the disorder of the alimentary tract. Probably the only means by which it will be found possible to check the excessive growth of the gastro-intestinal bacteria is that of the employment of specific antitoxins; and to avert the disease by such means may be more practicable than would at first sight appear, because it is probable that the specially injurious toxins are the products of only a few bacterial forms.

These contributions are very interesting and are most stimulating to further researches in the direction pointed out by Dr. Bruce's work. While not yet conclusive these results are consistent with the general trend of opinion that the toxaemias are the intervening factors; and, for the present, it is along this line of research that our expectations are led. If they are verified as a substantial addition to our knowledge then we may be fairly placed on new ground in respect to mental diseases in general.

This discussion of the treatment of paresis was hardly expected, I presume, to lead to any definite conclusion; indeed the statement of the subject suggests speculative inquiry. But still

we are on firm foundations, upon the principles of bacteriology and physiological chemistry. There are several by-products of such a study as this. We are shown the limitations of pathological anatomy, that instead of expecting to find explanations of mental symptoms in terms of structure, we must seek in the deeper plane of the chemistry of nutrition explanations of both function and structure, and the changes in them. We see that the final test of all observation, hypothesis and theory, is treatment; that we who minister to the sick must apply all the needed knowledge that can be gained; that we, with our problem in the living patient, do right to exalt the clinic, for the uses of which we may claim all the contributions of expert research. It is in the arena of the clinic that the patient and the physician are the leading players in the game of life and death.

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